



PC18174A

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

APPLICANT : M. DEVALARAJA, ET AL. EXAMINER : M. BELYAVSKYI  
SERIAL NO: 09/885,259 ART UNIT : 1644  
FILED: FEBRUARY 23, 2001 PAPER NO :  
FOR: INHIBITORS OF COLONY STIMULATING FACTORS

**DECLARATION OF JAMES L. MOBLEY UNDER 37 C.F.R. § 1.132**

I, James L. Mobley, do hereby make the following declarations:

1. I am an Associate Research Fellow in the Inflammation Pharmacology Department of Pfizer Global Research and Development at 2800 Plymouth Road, Ann Arbor, MI, 48105.
2. I have been employed as a pharmacologist at Pfizer Inc. and a company acquired by Pfizer Inc., Warner-Lambert Inc., since 1997.
3. In 1984, I earned my B.S. from the University of Illinois, Urbana-Champaign in Biology.
4. In 1987, I earned my M.S. from the University of Illinois, Urbana-Champaign in Biology.
5. In 1991, I earned my Ph.D. from the University of Iowa, Iowa City in Immunology.
6. A copy of my curriculum vitae is attached as Exhibit A.
7. I have read the contents of the Office Action in 09/885,259 and in particular the Examiner's rejection of claims 12, 14, 33-34, 36-37, 39, 41-42, and 44-50 under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled.

8. The Collagen Monoclonal Antibody-Induced Arthritis assay is a mouse model of rheumatoid arthritis which involves injecting a cocktail of monoclonal antibodies to type II collagen epitopes into a mouse to induce arthritis.
9. The Collagen Monoclonal Antibody-Induced Arthritis assay was known to those of skill in the art at least since 1995 as evidenced by the publication of Terato et al. (1992) *J. Immunol.* 148: 2103-2108 and Terato et al. (1995) *Autoimmunity* 22(3):137-147.
10. The present application (filed February 23, 2001) claims priority to a provisional patent application filed on filed March 20, 2000 - United States Serial No. 60/190,842.
11. Therefore, Terato et al. (1992), Terato et al. (1995), and the Collagen Monoclonal Antibody-Induced Arthritis assay were in the public domain at the time provisional application and the present application were filed.
12. The Collagen Monoclonal Antibody-Induced Arthritis assay is commonly carried out under my supervision in my laboratory to assess the effects of compounds for their activity as rheumatoid arthritis therapeutics.
13. In my opinion, the murine Collagen Monoclonal Antibody-Induced Arthritis model reasonably correlates to human rheumatoid arthritis.
14. The following three experiments, Experiments 1, 2, and 3, were carried out under my supervision to test anti-M-CSF antibodies in the Collagen Monoclonal Antibody-Induced Arthritis assay in mice.

#### **Experiment #1**

15. Twelve Balb/c female mice, 6-8 weeks old, were divided into three groups of four animals each - Group A, Group B, and Group C.

16. A cocktail of four type II collagen epitope antibodies, Arthrogen-CIA® Monoclonal Antibody Cocktail, is commercially available for use in the Collagen Monoclonal Antibody-Induced Arthritis model from CHEMICON International, Inc., Temecula, CA.
17. On day 0 of the experiment, each of the mice in all of the groups were injected intra-peritoneally with 400 µl (4 mg) of Arthrogen-CIA® Monoclonal Antibody Cocktail to induce arthritis.
18. On day 1 post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration the mice were injected intra-peritoneally with 400 µl of phosphate-buffered saline containing 50 µg of the respective antibody for that group:
  - Group A - normal goat IgG Control (R&D Systems Inc., Minneapolis, MN, Catalog number Cat # AB-108-C);
  - Group B - polyclonal goat anti-mouse TNF- $\alpha$  antibody (R&D Systems Inc., Minneapolis, MN, Catalog number AF-410-NA); and
  - Group C - polyclonal goat anti-mouse M-CSF antibody (R&D Systems Inc., Minneapolis, MN, Catalog number AB-416-NA).
19. On day 2 post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration each of the mice was injected intra-peritoneally with 200 µl lipopolysaccharide (LPS) (250 µg/ml; derived from E. coli strain 0111B4).
20. On day 4 post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration the respective groups were injected intra-peritoneally with 400 µl of phosphate-buffered saline containing 50 µg of the respective antibody for that group:
  - Group A - normal goat IgG Control (R&D Systems Inc., Minneapolis, MN, Catalog number Cat # AB-108-C);
  - Group B - polyclonal goat anti-mouse TNF- $\alpha$  antibody (R&D Systems Inc., Minneapolis, MN, Catalog number AF-410-NA); and

Group C - polyclonal goat anti-mouse M-CSF antibody (R&D Systems Inc., Minneapolis, MN, Catalog number AB-416-NA).

21. All of the groups were assayed for paw swelling using a Dyer Digital Caliper (#655-030-4916) on days 0, 2, 5, 8, 10, and 12.
22. A Change score is the sum of the differences between the width (in millimeters) of all four paws and the two rear ankles of a mouse on day 0 and the width of all four paws and the two rear ankles of that same mouse on a later day in the experiment (e.g., day 2, day 5, day 8, day 10 and day 12).
23. The mean change score  $\pm$  the standard error of the mean for each group versus the day post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration is graphed in Exhibit B (attached).
24. The mean change score for the M-CSF antibody treated group (Group C) is lower than the mean change score for the control normal goat IgG antibody treated group (Group A) for days 8 and 10 (see Exhibit B).
25. The lower mean change score of the polyclonal M-CSF antibody AB-416-NA treated group (Group C) as compared to the control normal IgG antibody treated group (Group A) for days 8 and 10 indicates that the M-CSF antibody administration is able to decrease the severity of the Collagen Monoclonal Antibody-Induced Arthritis.

## **Experiment #2**

26. Twenty female Balb/c mice, 6-8 weeks old, were divided into 5 groups of four animals each - Group D, Group E, Group F, Group G, and Group H.
27. On day 0 of the experiment, each of the mice in all of the groups were injected intra-peritoneally with 400  $\mu$ l (4 mg) of Arthrogen-CIA® Monoclonal Antibody Cocktail to induce arthritis.

28. On day 1 post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration the respective groups were injected intra-peritoneally with:
- Group D - phosphate-buffered saline (PBS);
  - Group E - mouse anti-mouse M-CSF monoclonal antibody 2A9.B9 (1 mg);
  - Group F - mouse anti-mouse M-CSF monoclonal antibody 2C2.B10 (1 mg);
  - Group G - mouse anti-mouse M-CSF monoclonal antibody 3C4.C9 (1 mg); and
  - Group H - mouse anti-mouse M-CSF monoclonal antibody 4D8.D6 (500 µg).
29. The mouse anti-mouse M-CSF monoclonal antibodies, 2A9.B9; 2C2.B10; 3C4.C9; and 4D8.D6 were isolated from hybridomas generated by Green Mountain Inc. (Burlington, VT). The hybridomas were obtained using standard hybridoma technology from M-CSF null mice that had been injected with mouse M-CSF.
30. On day 2 post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration each of the mice was injected intra-peritoneally with 100 µl LPS (250 µg/ml; derived from E. coli strain 0111B4).
31. All of the groups were assayed for paw swelling using a Dyer Digital Caliper (#655-030-4916) on days 0, 2, 4, 7, 9, and 11 to generate a mean change score as described above in ¶22.
32. The mean change score  $\pm$  the standard error of the mean for each group versus the day post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration is graphed in Exhibit C (attached).
33. On Days 4, 7 and 9, Group E (monoclonal antibody 2A9.B9 (1 mg dose)) exhibited a lower mean change score as compared to the PBS control group (Group D).

34. On Days 4, 7, 9 and 11, Group F (monoclonal antibody 2C2.B10 (1 mg dose)) exhibited a lower mean change score as compared to the PBS control group (Group D).
35. On Day 4, Group G (monoclonal antibody 3C4.C9 (1 mg dose)) exhibited a lower mean change score as compared to the PBS control group (Group D).
36. On Days 4, Group H (monoclonal antibody 4D8.D6 (500 µg dose)) exhibited a lower mean change score as compared to the PBS control group (Group D).

### **Experiment #3**

37. Fifteen 6-8 weeks old female Balb/c mice were divided into 3 groups: Group I, Group J, and Group K.
38. Seven days prior to Arthrogen-CIA® Monoclonal Antibody Cocktail administration and 1 day prior to Arthrogen-CIA® Monoclonal Antibody Cocktail administration, the Group J mice were each injected intra-peritoneally with 100 µg of rat anti-mouse M-CSF monoclonal antibody (R&D Systems Inc., Minneapolis, MN, Catalog number MAB416).
39. One hour prior to Arthrogen-CIA® Monoclonal Antibody Cocktail administration the Group K mice were each injected intra-peritoneally with 100 µg of MAB416.
40. On day 0 of the experiment, each of the mice in all of the groups were injected intra-peritoneally with 400 µl (4 mg) of Arthrogen-CIA® Monoclonal Antibody Cocktail to induce arthritis.
41. On day 2 post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration each of the mice was injected intra-peritoneally with 100 µl LPS (250 µg/ml; derived from E. coli strain 0111B4).

42. All of the groups were assayed for paw swelling using a Dyer Digital Caliper (#655-030-4916) on days 0, 2, 4, 7, 9, 11, and 14 to generate a mean change score as described above in ¶22.
43. The mean change score  $\pm$  the standard error of the mean for each group versus the day post-Arthrogen-CIA® Monoclonal Antibody Cocktail administration is graphed in Exhibit D (attached).
44. On Days 7, 9, and 11 the Group K mice which were administered monoclonal antibody MAB416 (100  $\mu$ g dose) one hour prior to Arthrogen-CIA® Monoclonal Antibody Cocktail administration exhibited a lower mean change score as compared to the mice of Group I.
45. The Group J mice which were administered monoclonal antibody MAB416 (100  $\mu$ g dose) 7 days and 1 day prior to Arthrogen-CIA® Monoclonal Antibody Cocktail administration did not exhibit a lower mean change score as compared to the mice of Group I.

## CONCLUSION

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: September 14, 2004

By: \_\_\_\_\_

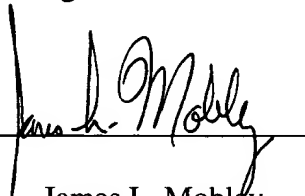
  
James L. Mobley



Exhibit A

**CURRICULUM VITAE**

James L. Mobley

Pfizer Global Research and Development  
2800 Plymouth Road  
Ann Arbor, MI 48105

**EDUCATION**

Ph.D.	Immunology University of Iowa, Iowa City December, 1991
M.S.	Biology (GPA 3.92/4.00) University of Illinois, Urbana-Champaign May, 1987
B.S.	Biology (GPA 3.83/4.00) University of Illinois, Urbana-Champaign May, 1984
A.S.	Wabash Valley College, Mt. Carmel, IL May, 1982 GPA 3.93/4.00

**POSTGRADUATE TRAINING**

Intramural NIH Postdoctoral Training Grant Fellowship, Department of Pathology, The University of Iowa College of Medicine, Iowa City, IA, 1992.

Cancer Research Institute Postdoctoral Fellowship, Department of Microbiology and Immunology, The University of Michigan School of Medicine, Ann Arbor MI/The University of Minnesota Dept. of Lab Medicine and Pathology, Minneapolis, MN, from 1992 to 1995 under the direction of Dr. Yoji Shimizu.

Post-doctoral Research Scientist, Cell Biology and Inflammation Research Unit, Pharmacia & Upjohn, Inc., Kalamazoo, MI, 11/6/95 to 4/11/97.

## POSITIONS HELD

Associate Research Fellow, Inflammation Pharmacology, Pfizer Global R & D, 2002-present  
Research Associate, Inflammation Therapeutics, PGRD, 2000-2002  
Senior Scientist, Immunopathology, Parke-Davis Pharmaceutical Research, 1997-2000

## HONORS and AWARDS

Phi Theta Kappa Honor Society, 1982  
Phi Kappa Phi Honor Society, 1983  
Outstanding Student Award, Wabash Valley College, 1982  
Student Senate President, Wabash Valley College, 1982  
Illinois Eastern Community College School Board, student representative, 1982  
Microbiology Graduate Student Organization, president, 1990

## PROFESSIONAL AFFILIATIONS

American Association for the Advancement of Science  
American Association of Immunologists  
Ad hoc reviewer for the Journal of Immunology

## INVITED PROFESSIONAL DUTIES

Workshop Chairman, "Lymphocyte Trafficking and Adhesion", Autumn Immunology Conference, Chicago, IL, 1997.  
Block Symposium Co-chairman, "Inflammation and Inflammatory Diseases", Federation of American Societies for Experimental Biology meeting, Washington D.C, 1999.  
Symposium Chairman, "Pattern Recognition Receptors in Inflammation", Autumn Immunology conference/Inflammation Research Association, Chicago, 2003.  
Symposium Co-chairman, "Innate Immunity", Inflammation Research Association International Conference, Lake George, NY 2004.

## GRANTS AWARDED

Cancer Research Institute Postdoctoral Fellowship "Intracellular requirements for activation-dependent regulation of VLA integrin function" 1/1/93-10/31/95  
Arthritis Foundation Postdoctoral Fellowship, 1993. Declined in favor of Cancer Research Institute Fellowship  
The Irvington Institute for Medical Research Postdoctoral Fellowship, 1993. Declined in favor of Cancer Research Institute Fellowship  
NIH Public Health Service Postdoctoral Fellowship, 1993. Declined in favor of Cancer Research Institute Fellowship.

## Exhibit A

### TEACHING EXPERIENCE

Teaching Assistant, Introduction to Immunology (G&D 307), The University of Illinois 1985-87. Duties included preparation and presentation of a lecture/discussion on basic immunology to upper level undergraduates and graduate students.

Teaching Assistant, General Microbiology Lab, The University of Iowa, 1987-1991. Duties included overseeing an introductory microbiology lab course 4 hours/day, 2 days/week, 1 semester/year. Students included Medical, Dental, Physician Asst. and Nursing students.

### THESES DIRECTED

James T. Wise, M.S. (Eastern Michigan University) - Adoptive transfer of allergic lung inflammation in mice.

### PUBLICATIONS

1. Mobley, J. L., and M. O. Dailey. 1991. Regulation of adhesion molecule expression by antigen-specific T cells in vivo. In *Lymphatic Tissues and In Vivo Immune Responses*. B. A. Imhoff, S. Berrih-Aknin, and E. Ezine, eds. Marcel Dekker, Inc., New York, NY, pp. 915-920.
2. Mobley, J. L., and M. O. Dailey. 1992. Regulation of adhesion molecule expression by CD8 T cells in vivo. I. Differential regulation of gp90<sup>MEL-14</sup> (LECAM-1), Pgp-1, LFA-1, and VLA-4 $\alpha$  during the differentiation of cytotoxic T lymphocytes induced by allografts. *J. Immunol.* 148: 2348-2356.
3. Mobley, J., G. Evans, M. O. Dailey, and S. Perlman. 1992. Immune response to a murine Coronavirus: Identification of a homing receptor-negative CD4 T cell subset that responds to viral glycoproteins. *Virology* 187: 443-452.
4. Mobley, J. L., S. Rigby, and M. O. Dailey. 1994. Regulation of adhesion molecule expression by CD8 T cells in vivo. II. Expression of L-selectin (CD62L) by memory cytolytic T cells responding to minor histocompatibility antigens. *J. Immunol.* 153: 5443-5452.
5. Mobley, J. L., P. J. Reynolds, and Y. Shimizu. 1993. Regulatory mechanisms underlying T cell integrin receptor function. *Seminars in Immunology* 5: 227-236.
6. Shimizu, Y., and J. L. Mobley. 1993. Distinct divalent cation requirements for integrin

- mediated CD4 T lymphocyte adhesion to ICAM-1, fibronectin, VCAM-1, and invasin. *J. Immunol.* 151: 4106-4115.
7. Reynolds, P. J., J. L. Mobley, and Y. Shimizu. 1993. Lymphocytes and extracellular matrix. In *Lymphocyte Adhesion Molecules*. Y. Shimizu ed. R. G. Landes Company, Austin, TX.
  8. Mobley, J. L., E. Ennis, and Y. Shimizu. 1994. Differential activation-dependent regulation of integrin function in cultured human T leukemic cell lines. *Blood* 83: 1039-1050.
  9. Mobley, J. L. and Y. Shimizu. 1994. Measurement of cellular adhesion under static conditions. In *Current Protocols in Immunology*, J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, and W. Strober, eds. Greene Publishing Associates, New York, NY, (Unit 7.28).
  10. Mobley, J. L., N. C. Romzek, and Y. Shimizu. 1996. Integrin activation in lymphocyte adhesion. In *Handbook of Experimental Immunology*, Blackwell Scientific Publications, Cambridge, (Chapter 68).
  11. Mobley, J. L. E. Ennis, and Y. Shimizu. 1996. Isolation and characterization of cell lines with genetically distinct mutations downstream of protein kinase C that result in defective activation-dependent regulation of T cell integrin function. *J. Immunol.* 156: 948-956.
  12. Shimizu, Y., J. L. Mobley, L. D. Finkelstein, and A. S. H. Chan. 1996. A role for phosphatidylinositol 3-kinase in the regulation of  $\beta 1$  integrin activity by the CD2 antigen. *J. Cell Biol.* 131: 1867-1880.
  13. Zell, T., S. W. Hunt III, J. L. Mobley, L. D. Finkelstein, and Y. Shimizu. 1996. CD28 mediated upregulation of  $\beta 1$  integrin adhesion involves phosphatidylinositol 3-kinase. *J. Immunol.* 156: 883-886.
  14. Mobley, J. L., J. E. Chin, and I. M. Richards. 1996. Glucocorticoids, old and new: biological function and use in the treatment of asthma. *Expert Opinion on Investigational Drugs* 5: 871-884.
  15. Mobley, J. L., J. E. Chin, and I. M. Richards. 1997. Cytokine networks in allergic lung inflammation. *Expert Opinion on Investigational Drugs* 6:1-6.
  16. Hatfield, C. A., J. R. Brashler, G. E. Winterrowd, F. P. Bell, R. L. Griffin, S. F. Fidler, K. P. Kolbassa, K. L. Shull, J. L. Mobley, I. M. Richards, and J. E. Chin. 1997. Intercellular adhesion molecule-1 deficient mice have antibody responses but impaired leukocyte recruitment. *Am. J. Physiol.* 273: L513-L523.

#### Exhibit A

17. Chan, A. S. H., J. L. Mobley, G. B. Fields, and Y. Shimizu. 1997. CD7-mediated regulation of integrin adhesiveness on resting human T cells involves tyrosine phosphorylation-dependent activation of phosphatidylinositol 3-kinase. *J. Immunol.* 159: 934-942.
18. Kivens, W. J., S. W. Hunt III, J. L. Mobley, T. Zell, C. L. Dell, B. E. Bierer, and Y. Shimizu. 1998. Identification of a proline-rich sequence in the CD2 cytoplasmic domain critical for regulation of integrin-mediated adhesion and activation of phosphatidylinositol 3-kinase. *Mol. Cell. Biol.* 18: 5291-5307.
19. Chen, C., J. L. Mobley, O. Dwir, F. Shimron, Vgrabovosky, R. R. Lobb, Y. Shimizu, and R. A. Alon. 1999. High affinity VLA-4 subsets expressed on T cells are mandatory for spontaneous adhesion strengthening but not for rolling on VCAM-1 in shear flow. *J. Immunol.* 162: 1084-1095.
20. Wise, J. T., T. J. Baginski, and J. L. Mobley. 1999. An adoptive transfer model of allergic lung inflammation in mice is mediated by CD4<sup>+</sup>CD62L<sup>low</sup>CD25<sup>+</sup> T cells. *J. Immunol.* 162: 5592-5600.
21. Bullard, D. C., J. L. Mobley, L. A. Hurley, J. M. Justen, L. M. Sly, J. G. Chosay, C. J. Dunn, J. R. Lindsey, A. L. Beaudet, and N. D. Staite. 1999. Acceleration and increased severity of collagen-induced arthritis in P-selectin deficient mice. *J. Immunol.* 163: 2844-2849.
22. Mobley, J.L. 2004. Is rheumatoid arthritis a consequence of natural selection for enhanced tuberculosis resistance? *Medical Hypotheses* 62:839-843.

#### PATENTS

1. U.S. Patent No. 6,696,440 - Treatment of asthma with MEK inhibitors.

#### ABSTRACTS and PRESENTATIONS

1. Mobley, J. L., and M. O. Dailey. Down-regulation of homing receptor expression on CTL activated in vivo. Abstract published and presented at a poster session at the Federation of American Societies for Experimental Biology meeting, Atlanta, GA. 1990.
2. Mobley, J. L., and M. O. Dailey. Adhesion molecule expression identifies the state of differentiation of CD8 T cells. Abstract published and presented at a poster session at the Federation of American Societies for Experimental Biology meeting, New Orleans, LA. 1991.
3. Dailey, M. O., M. Comito, and J. L. Mobley. Regulation of adhesion molecule expression

during the activation and differentiation of T cells in vivo. Abstract published and presented at a poster session at the Federation of American Societies for Experimental Biology meeting, New Orleans, LA. 1991.

4. Mobley, J. L., S. M. Rigby, and M. O. Dailey. Adhesion molecule expression on effector and memory CD8 T cells in vivo. Abstract published and presented at a poster session at the Federation of American Societies for Experimental Biology meeting, Anaheim, CA. 1992.
5. Mobley, J. L., S. M. Rigby, and M. O. Dailey. L-selectin expression by memory cytotoxic T cells in vivo. Abstract presented at the 8th International Congress of Immunology, Budapest, Hungary, 1992.
6. Mobley, J. L. and Y. Shimizu. Differential activation-dependent regulation of integrin function in cultured human T cell lines. Poster presented at the Gordon Research Conference on Cell Contact and Adhesion, Andover, NH. 1993.
7. Mobley, J. L., E. Ennis, and Y. Shimizu. A mutational analysis of the activation dependent regulation of human T cell integrin function. Poster presented at the Midwest Autumn Immunology Conference, Chicago, IL. 1994.
8. Mobley, J. L. and Y. Shimizu. CD2-mediated activation of MAP kinase is dependent on phosphatidylinositol 3-kinase function. Poster presented at the Midwest Autumn Immunology Conference, Chicago, IL. 1995.
9. Mobley, J. L., C. A. Hatfield, K. P. Kolbasa, I. M. Richards, and J. E. Chin. Inhibition of antigen-induced murine lung inflammation by peritonitis induction concurrent with immunization. Presented at The American Thoracic Society meeting, San Francisco, CA. 1997.
10. Mobley, J. L., C. A. Hatfield, J. R. Brashler, S. F. Fidler, I. M. Richards, and J. E. Chin. Elevated Th2-mediated immune response to inhaled antigen in mice genetically deficient in P-selectin expression. Presented at The American Thoracic Society meeting, San Francisco, CA. 1997.
11. Mobley, J. L., J. T. Wise, T. J. Baginski, and M. R. Raynor. An adoptive transfer model of allergic lung inflammation in mice is mediated by CD4<sup>+</sup>CD62L<sup>low</sup>CD25<sup>+</sup> T cells. Presented at the Federation of American Societies for Experimental Biology meeting, Washington D.C., 1999.
12. Gilbertsen, R. B., K. P. Chan, C. A. Vento, T. J. Baginski, M. Raynor, H. Tecle, D. Dudley, and J. L. Mobley. Potent inhibition of T cell activation and cytokine production by the MEK inhibitor PD 184352: Efficacy in a murine asthma model following continuous dosing.

Exhibit A

Keystone symposium on T cell stimulation, activation, and death. 2000.

13. Spencer, N. F. L, M. Raynor, and J. L. Mobley. Subset-specific migration of CD4 T cells into the lungs of ovalbumin-challenged mice. Presented at the Federation of American Societies for Experimental Biology meeting, Washington D.C, 2000.

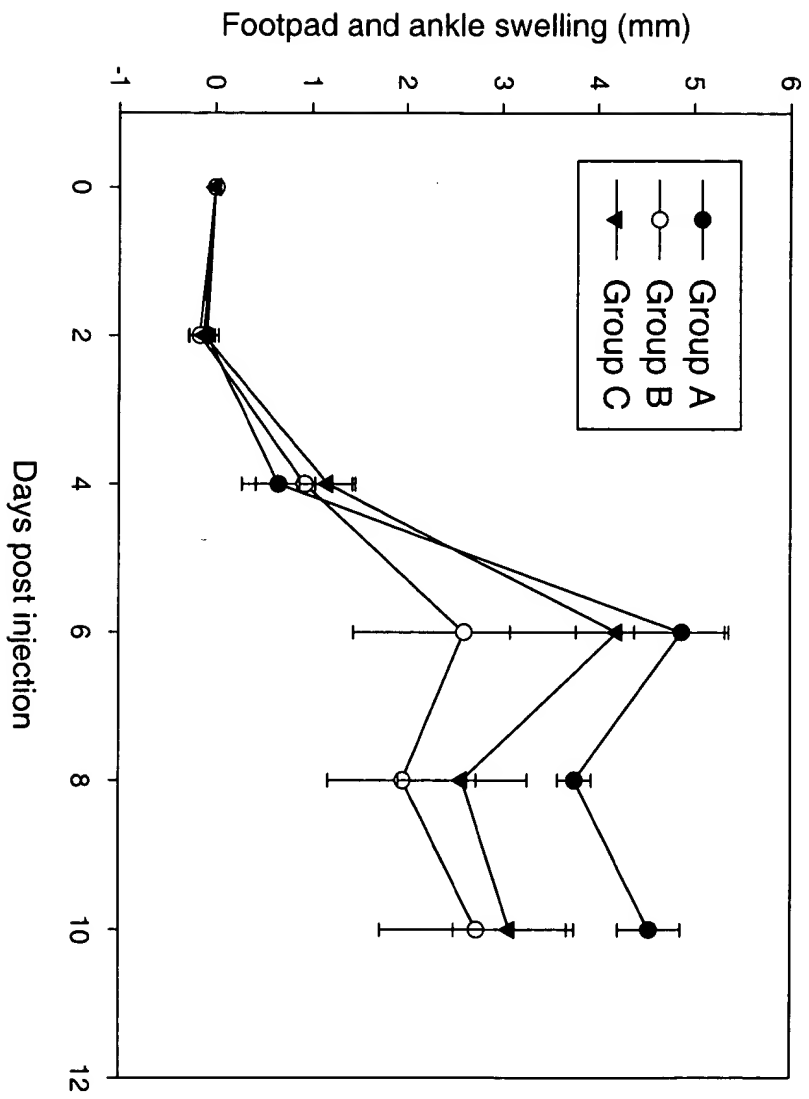
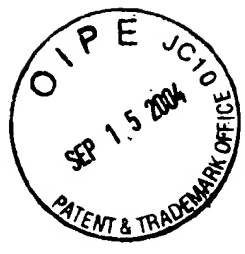
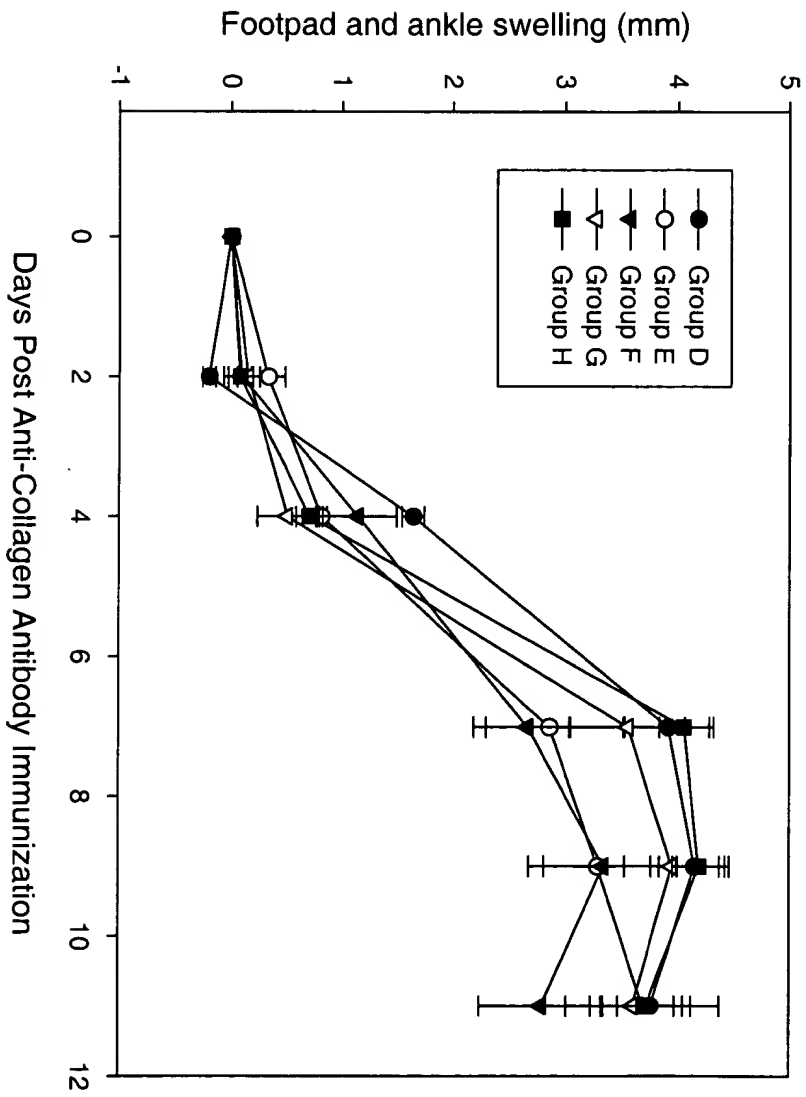


Exhibit B





Exhibit C



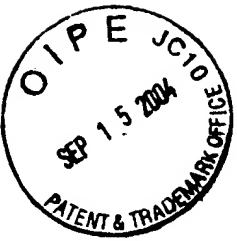


Exhibit D

